

### REMARKS

Favorable reconsideration is respectfully requested in view of the above amendments and the following remarks. Following the amendments, claims 175-196 are pending in the application, with claims 175 and 186 being in independent format.

The previously pending claims have been cancelled from the application and new claims 175-196 have been added. Independent claim 175 is drawn to *in vitro* methods for the generation of cartilage tissue from cells expressing the mechanosensitive TREK potassium ion channel comprising: (a) providing magnetizable particles that are tagged with an antibody specific for the TREK ion channel, (b) contacting the magnetizable particles with cartilage cells expressing the TREK ion channel and allowing the magnetizable particles to couple with the TREK ion channel through binding of the antibody to the TREK ion channel, and (c) applying a magnetic field to the cells such that the magnetizable particles, and cells coupled to the particles, experience an applied mechanical force that activates the TREK ion channel causing a second messenger pathway to be triggered that leads to growth of cartilage tissue. Independent claim 186 is directed to similar methods for the generation of new cartilage tissue in a patient.

It is urged that support for the newly added claims may be found throughout the specification as originally filed. More specifically, support for independent claim 175 may be found, for example, at page 3, line 31 to page 4, line 8; page 4, lines 29-30; page 5, lines 6-9, 11-22 and 28-29; page 6, lines 20-24; page 7, lines 5-8; page 8, lines 1-6 and 9-11; page 9, lines 13-16; page 10, line 27; and in Example 4 of the specification as filed. Support for independent claim 186 may be found, for example, at page 3, line 31 to page 4, line 8; page 5 lines 6-9 and 11-22; page 7, lines 5-8; page 8 lines 4-6; page 9, lines 1-2 and 13-16; and page 10, line 27.

Support for the dependent claims may be found, for example, as follows: claim 176 – page 9, line 15; claims 177 and 188 – page 9, lines 9-10; claims 178 and 189 – page 5, line 20 and Example 4; claims 179 and 190 – page 10, line 21; claims 180 and 191 – page 10, line 23; claims 181 and 192 – page 7, line 20; claims 182 and 193 – page 7 line 2; claims 183 and 194 – page 7, lines 2-4; claims 184 and 195 – page 7, lines 4-5; claims 185 and 196 – page 7, lines 4-5; and claim 187 – page 9, line 18.

It is urged that support for all the above amendments can be found throughout the application as originally filed and that none of the amendments constitute new matter or raise new issues for consideration.

### **Claim Objections**

The Examiner had objected to claims 28, 32, 46 and 47 as containing minor informalities. As noted above, claims 28, 32, 46 and 47 have been cancelled from the application, thereby rendering the objections moot.

### **Claim Rejections under 35 USC §112, first paragraph – Written Description**

Claims 26, 28-29, 31, 32, 36, 37, 39, 40, 43, 45, 46, 49, 50, 59-64, 68, 69, 71 and 154-174 were finally rejected under 35 USC §112, first paragraph, as lacking an adequate written description. As noted above, these claims have been cancelled from the application, thereby rendering this rejection moot. Applicants will, however, address the Examiner's grounds for rejection of the cancelled claims to the extent that they may be applied to newly added claims 175-196.

### **Maintained rejections**

Following the above amendments, the pending claims are directed to generation of cartilage tissue using magnetizable particles tagged with an anti-TREK antibody. It is urged that the specification as originally filed provides an adequate written description of these features and clearly indicates that the applicant was in possession of the claimed invention at the time the application was filed. The generation of cartilage tissue using magnetizable particles tagged with the anti-TREK antibody is further supported by the declaration of Professor El Haj submitted on January 8, 2008.

More specifically, at page 4 of the final Office Action, the Examiner asserts that applicants are not in possession of the previously claimed methods because, for instance, information regarding the molecules and cells involved in the treatment methods is not provided. The amended claims are directed to generation of cartilage tissue through contact of magnetizable particles having a biocompatible coating and tagged with an antibody specific for

TREK with cartilage cells expressing TREK. The cells, molecules and particles employed in the methods now claimed are clearly defined in the claims and are clearly described in the description.

Also on page 4 of the final Office Action, the Examiner asserts that correlation of the structural and functional characteristics of the disorder, ion channels and magnetizable particles is not provided. The amended claims are directed to a specific group of magnetizable particles that are tagged with TREK antibodies and are contacted with cartilage cells expressing TREK for the generation of new cartilage tissue. Function and structure is accurately correlated in these claims through the recitation of magnetizable particles tagged with TREK antibodies which structurally and functionally recognize the TREK ion channel expressed on the cartilage cells such that the magnetizable particles bind to the cells. Application of a magnetic field provides a mechanical force which activates the ion channel and triggers a second messenger pathway that has been shown to lead to an increase in expression of osteopontin and production of cartilage tissue, as described, for example, in the Declaration of Professor El Haj.

In response to the Examiner's further comments on page 4 of the final Office Action, applicants have amended the claims to clearly provide identifying characteristics of the method, the ion channel and magnetizable particle. The amended claims correspond to the description of the use of TREK tagged magnetizable particles to generate new cartilage tissue, whether *in vitro* or *in vivo*. The application clearly describes the component products and method steps of the amended claims. The application also describes specific methodology for the use of TREK tagged magnetizable particles in, for example, Examples 1 and 4.

It is urged that one of skill in the art would appreciate that the applicants were indeed in possession of the presently claimed invention at the filing date of the instant application. Furthermore, the application clearly describes magnetisable particles having a biocompatible coating and TREK antibody tag, contact of those particles with cartilage cells, application of a magnetic force to cells that have been allowed to couple with the TREK antibody tagged particles and the generation of cartilage tissue, and therefore discloses sufficient information to put the public in possession of the invention now claimed.

New grounds of rejection

In the final Office Action, the Examiner raised a new ground of rejection regarding previous claims 26, 28-29, 31-32, 36-37, 39-40, 43, 45 and 154-174. Specifically, the Examiner indicated that these claims are genus claims which do not indicate distinguishing attributes shared by members of the genus and that the specification does not provide guidance as to what changes may be made. The rejection considers several claim features including the composition of the magnetizable particles and cellular elements to which an antibody may bind.

In the amended claims, the magnetizable particle is indicated to be one that has a biocompatible coating and which is tagged with a TREK antibody. This definition of the magnetizable particles removes any possible doubt about how the magnetizable particles should be constructed or modified in order to be useful in the invention claimed. The magnetizable particles recited in the claims now represent a specific set of particles characterized by having a magnetic core, a biocompatible coating and an anti-TREK antibody tag.

The magnetic core is described in detail in the application. For example, page 7, lines 5-14, refer to nanoparticles described in US Patent 6,548,264 which is incorporated by reference. A copy of this patent is submitted with this response. The patent describes nanoparticles having biocompatible silica coatings, methods for making such particles and for functionalizing them with a protein (*e.g.* an antibody) – *see e.g.*, col. 2, lines 9-39. In the present application, the description of the particles continues (page 7, lines 16-30) to describe the size and nature of the particles. The structural composition of the magnetic core of the particles is also clearly set out in the paragraph bridging pages 6 and 7.

It is submitted that the particles encompassed by the claims are no longer “highly variant” (final Office Action at page 6, 1<sup>st</sup> paragraph). A clear description of the particles is provided in the application as filed, including reference to US Patent 6,548,264. Applicants have accordingly provided a written description of a representative number of species of the particle genus now recited in the claims and have described the particles with reference to their structure, function and physical properties (*e.g.* metallic composition, size, shape, coating and functionalization). This description also correlates with the functional and structural features of the invention now claimed. As such, it is clear that applicant was in possession of the invention now claimed at the filing date of the application.

It is submitted that one of skill in the art would appreciate that the applicants were indeed in possession of the claimed invention at the time the application was filed, and that the presently pending claims therefore fully satisfy the written description requirements of 35 USC §112, first paragraph.

**Claim Rejections under 35 USC §112, first paragraph - enablement**

Claims 26, 28-29, 31, 32, 36, 37, 39, 40, 43, 45, 46, 49, 50, 59-64, 68, 69, 71 and 154-174 were finally rejected under 35 USC §112, first paragraph, as lacking an enabling disclosure. As noted above, these claims have been cancelled from the application, thereby rendering this rejection moot. Applicants will, however, address the Examiner's grounds for rejection of the cancelled claims to the extent that they may be applied to newly added claims 175-196.

The Examiner states, on page 7 of the final Office Action, that the specification is enabling for "(A) upregulation of osteopontin in response to a magnetic field in the presence of anti-TREK antibody bound to magnetic nanoparticles binding to TREK channel mesenchymal cells, and (B) the production of cartilage in mice by implanted human mesenchymal stem cells in the presence of magnetic nanoparticles bound to cells via an anti-TREK antibody in response to time varying magnetic fields".

Applicant has amended the claims to correlate with the subject matter which the Examiner has indicated is enabled, *i.e.* the generation of cartilage tissue using magnetizable particles bound to an anti-TREK antibody. The claimed subject matter now directly correlates with results showing the successful generation of cartilage tissue using magnetizable particles tagged with anti-TREK antibody. This removes the prospect of the skilled person having to perform any undue experimentation to practice the presently claimed invention.

It is urged that one of skill in the art, on being provided with the instant specification, would be able to carry out the claimed methods without undue experimentation, and that the presently pending claims therefore fully satisfy the enablement requirement of 35 USC §112, first paragraph.

**Claim Rejections under 35 USC §112, Second Paragraph**

Claims 26, 28-29, 31, 32, 36, 37, 39, 40, 43, 45, 46, 49, 50, 59-64, 68, 69, 71 and 154-174 were finally rejected under 35 USC §112, second paragraph, as being indefinite. These claims have been cancelled from the application. Furthermore, the term objected to by the Examiner, namely “manipulating”, does not appear in the currently pending claims. It is therefore submitted that, following the above amendments, the pending claims fully satisfy the requirements of 35 USC §112, second paragraph

**Claim Rejections under 35 USC §102**

Claim 46 was finally rejected under 35 USC §102 as being anticipated by Yanase et al. (Jpn. J. Cancer Res. 89:463-469, 1998). As noted above, claim 46 has been cancelled from the application, thereby rendering this rejection moot.

Applicants submit that Yanase et al. do not teach a method of generating cartilage tissue by contacting cartilage cells with magnetisable particles tagged with an anti-TREK antibody, as recited in the amended claims, and that the amended claims are therefore novel over Yanase et al. Furthermore, it is submitted that the teachings of Yanase et al. would not have rendered the currently claimed subject matter obvious to one of skill in the art at the time the invention was made. It is thus urged that the pending claims fully satisfy the requirements of 35 USC §§102 and 103.

**Concluding Remarks**

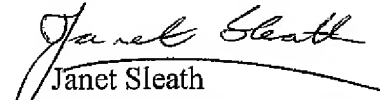
A Request for a Three Month Extension of Time, extending the deadline for responding to the final Office Action to October 15, 2008, is submitted herewith.

Every effort has been made to put the pending claims in condition for allowance. Favorable reconsideration and early allowance of all the pending claims is respectfully requested.

Application No. 10/518,956  
Amendment dated October 14, 2008  
Reply to Final Office Action mailed April 15, 2008

Should the Examiner have any further concerns regarding this application, he is requested to telephone the undersigned at 206.382.1191.

Respectfully submitted,

  
Janet Sleath  
Registration No. 37,007

**SPECKMAN LAW GROUP PLLC**  
**20601**